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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/437,726	11/09/1999	WILLEM P. C. STEMMER	02-029220US	8363

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	09/437,726	STEMMER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-19,21-27 and 31-37* is/are pending in the application.

4a) Of the above claim(s) *10-19 and 21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27 and 31-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 02 March 2004 has been entered.

Specification

2. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states: "All publications cited are incorporated herein by reference, whether specifically noted as such or not." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference from each and every document cited and similarly fails to teach with detailed particularity just where that specific information is to be found in each of said cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that**

> **material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code; see page 3, line 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. It is noted that applicant, at page 6 of their response of 09 October 2001 assert that hyperlinks have been deleted, however, the hyperlink found at this page does not appear to have been treated.

Priority

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 27 and 31-37 of this application.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 27 and 31-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

8. For convenience, claim 27, the sole independent claim under consideration, is reproduced below.

> Claim 27 (previously presented) A method for obtaining an isolated polynucleotide comprising a sequence encoding a protein having Rubisco carboxylation activity, the method comprising:
>
> recombining a plurality of parental polynucleotide species encoding at least one protein having Rubisco carboxylation activity under conditions suitable for sequence shuffling to form a resultant library of sequence-shuffled polynucleotides;
>
> transferring said library into a plurality of host cells, thereby forming a library of transformants wherein sequence-shuffled Rubisco polynucleotides are expressed;
>
> identifying at least one transformant from said library that expresses an enhanced protein having a Rubisco carboxylation activity that is enhanced to an extent that is statistically significant relative to the Rubisco carboxylation activity of proteins encoded by the plurality of parental polynucleotide species, wherein the identified transformant contains a polynucleotide comprising a sequence encoding the enhanced protein; thereby obtaining a polynucleotide comprising a sequence encoding the enhanced protein.

9. For purposes of examination, claim 27 has been interpreted as encompassing the modification of an infinite number "parental polynucleotide species" that encode any polypeptide that has any level of RUBISCO (ribulose-1,5-bis-phosphate carboxylase) carboxylation activity. While claims 33-37 stipulate that the parent polynucleotide encodes a certain subunit, the specification does not provide an adequate written description of the amino acids that the various subunits, or their equivalents, are comprised of.

10. Said claim 27, and claims 31-37, which depend therefrom, have also been interpreted as encompassing the production and screening of an infinite number of transformants. The originally filed application does not support the position that applicant was in possession of a method whereby any number of transformants could be screened. In support of this position, attention is directed to page 3 of the Declaration of Genhai Zhu Pursuant to 37 CFR 1.132 on 13 November 2002, where is stated: "It would be physically impossible to screen more than a tiny

fraction of [1 x 10^{16}] cells." Therefore, in view of sworn statements of applicant's own declarant, and in the absence of convincing evidence to the contrary, the specification does not reasonably suggest that applicant had possession of the claimed invention at the time of filing.

11. In order to practice the claimed method, one must first have such "parental polynucleotide species." A review of the specification fails to find an adequate written description of any such parent polynucleotide species. Further, the specification does not provide an adequate written description of what polynucleotide sequences are essential to exhibiting any level of Rubisco carboxylation activity. While the specification does provide various citations, such citations have been improperly incorporated by reference and cannot therefore, be relied upon for satisfaction of the written description requirement.

12. For the above reasons, and in the absence of convincing evidence to the contrary, claims 27 and 31-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

13. Claims 27 and 31-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute

> even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

14. The claimed method fairly encompasses the production of polynucleotides that encode a protein that has virtually any increased level of RUBISCO (ribulose-1,5-bis-phosphate carboxylase) carboxylation activity. It is clear that in order to practice the claimed method, one must have a plurality of "parental polynucleotide species" where at least one of said parental polynucleotides encodes a polypeptide that exhibits Rubisco carboxylation activity. As presented above, the specification does not reasonably suggest that applicant was in possession of the claimed invention at the time of filing. It is well settled that one cannot enable an invention that they do not yet possess. Accordingly, and in he absence of convincing evidence to the contrary, claims 27 and 31-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

15. As noted above, the specification does not provide an adequate written description of the essential starting materials- the parental polynucleotides. Further, the specification does not

provide an adequate teaching of the structure-function relationship such that alternative parental polynucleotides could be used in the claimed process. In short, applicant has not provided the essential starting materials. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

Therefore, with no essential starting materials being provided, undue experimentation is required. Accordingly, and in the absence of convincing evidence to the contrary, claims 27 and 31-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 27 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patten et al. (*Current Opinion in Biotechnology*, Vol. 8, No. 6, December 1997, 724-733) and Jamet et al. (*Journal of Molecular Evolution*, 1991, Vol. 33, pp. 226-236).

Patten et al., teach at length of the benefits and broad applicability. In particular, Patten et al., at page 725, left column teach:

> DNA shuffling combined with focused selection pressure in the laboratory will allow one to rapidly evolve genes for a wide variety of industrial applications: the optimization of enzymes...

And at page 728:

> DNA shuffling allows one to directly recombine all beneficial mutations from any given round into multi-step mutants with dramatically improved phenotypes.

20. While Patten et al., teach of applying DNA shuffling to genes, including genes that exist in subunits, Patten et al., do not explicitly teach of performing DNA shuffling on the parental polynucleotides of RUBISCO (ribulose-1,5-bis-phosphate carboxylase).

21. Jamet et al., teach at length of the genes encoding RUBISCO (ribulose-1,5-bis-phosphate carboxylase), and subunits thereof.

22. Applicant at page 3 of the specification teaches:

> Because of the abundance and fundamental importance of Rubisco, the enzyme has been extensively studied. Well over 1,000 different Rubisco homologues are available in the public literature (e.g., over 1,000 different Rubisco homologues are listen [*sic*] in GenBank alone), and the crystal structure of Rubisco has been solved for several variants of the protein.

23. In view of the admitted well documented interest in RUBISCO, the "fundamental importance" that it possesses, one of ordinary skill in the art would have been motivated to have been amply motivated to have subjected parental polynucleotide species that encode RUBISCO to DNA shuffling such that optimized RUBISCO could be obtained and isolated. In view of the explicit guidance, and broad applicability of DNA shuffling to proteins in general, the ordinary artisan would have had a most reasonable expectation of success. Therefore, and in the absence of convincing evidence to the contrary, claims 27 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patten et al. (*Current Opinion in Biotechnology*, Vol. 8, No. 6, December 1997, 724-733) and Jamet et al. (*Journal of Molecular Evolution*, 1991, Vol. 33, pp. 226-236).

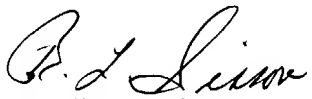
Conclusion

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

25. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

26. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
01 June 2004